Liu et al.

Serial No. 10/619,820

Page 2

- Claim 1. (Currently amended) A label-free method for the classification of eellular events,
  wherein the classification is achieved through measuring signal transduction from
  stimulus-receptor interactions by the measurement of changes in the electrical properties
  of cells incorporated into an electrical circuit after application of a stimulus,
  the method comprising:
  - (a) measuring a value of an electrical property <u>after application of for</u> at least one frequency <u>of the electromagnetic spectrum</u> within a range of frequencies for <u>each</u> selected time points during a selected period of time for <u>the electric circuit comprising</u> a cells with a receptor having a known receptor type and a known messenger pathway;
  - (b) selecting a reference time point corresponding to a time period immediately prior to addition of a known <u>receptor</u> stimulus;
  - (c) adding a the known stimulus to the electric circuit such that the stimulus is able to interact with the receptor;
  - (d) calculating changes in the value of the electrical property for each frequency by subtracting the value of the measured electrical property for the reference time point from the value of the measured electrical property for each <u>time point</u> subsequent <u>to the reference</u> time point;
  - (e) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
  - (f) and, comparing the parameterized changes in the value of the electrical property to parameter sets of known messenger pathways to assigning the parameterized changes in value of the electrical property to a known stimulus/receptor interaction class.

Liu et al. Serial No. 10/619,820

Page 3

Claim 2. (Canceled)

Claim 3. (Currently amended) The method of claim 1, wherein the electrical properties are

chosen from the group comprising comprise impedance phase, impedance magnitude, complex

reflection coefficients, total circuit resistance, and total circuit capacitance.

Claim 4 (Currently amended). The method of claim 1, wherein the at least one frequency

within a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic

frequencies.

Claim 5 (Currently amended). The method of claim 1, wherein the range of frequencies is

40Hz to 110MHz.

Claim 6 (Currently amended). The method of claim 1, wherein the stimulus is a substance.

Claim 7 (Canceled).

Claim 8 (Currently amended). The method of claim 6, wherein the substance is a ligand, a

protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

Claim 9 (Canceled).

Claim 10 (Currently amended).

The method of claim 1, further comprising the steps of

- g) measuring the value of the electrical property for the electric circuit comprising cells for at least one frequency in a range of frequencies for each selected time points during a selected period of time for a cell with a known receptor type;
- h) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;
- i) adding the unknown stimulus to the circuit such that the stimulus is able to interact with the receptor;
- j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each subsequent-time point subsequent to after addition of the unknown stimulus;
- k) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
- of the unknown stimulus to the <u>parameterized changes in value for known stimuli</u>

  changes in the value of the electrical properties for known stimuli to correlate the changes in the value of the electrical property to a cellular response;
- m) and, assigning the cellular response to the unknown stimulus to a known substance/receptor interaction class and classifying the stimulus.

Claim 11 (Currently amended). The method of claim 1, further comprising the steps of

- g) measuring the value of the electrical property for the electrical circuit comprising cells for at least one frequency within a range of frequencies for each selected time points during a selected period of time for a cell with an unknown receptor type;
- h) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus with a known response;
- i) adding the stimulus to the circuit such that the stimulus is able to interact with the receptor;
- j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each subsequent time point subsequent to after addition of the stimulus;
- k) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
- of the stimulus to the <u>parameterized</u> changes in the value of the electrical property after addition of the stimulus to the <u>parameterized</u> changes in the value of the electrical properties for known receptors to correlate the changes in the value of the electrical property to a cellular response;
- m) and, assigning the cellular response of the unknown receptor to a known substance/receptor interaction class and classifying the receptor.

Claim 12 (Currently amended). A label-free method for the classification of cellular events signal transduction from stimulus/receptor interactions,

wherein the classification is achieved through measuring changes in the <u>complex</u> impedance of cells <u>incorporated into an electrical circuit</u> after application of a <u>receptor</u> stimulus

the method comprising:

- a) measuring the <u>complex</u> impedance over at least one frequency <u>of the electromagnetic</u>

  <u>spectrum</u> in a range of frequencies for <u>each</u> selected time points during a selected period of time for the <u>electric circuit comprising</u> cells with a known receptor type and a known messenger pathway;
- b) selecting a reference time point corresponding to a time period immediately prior to addition of a known <u>receptor</u> stimulus;
- c) adding a the known stimulus to the electric circuit such that the stimulus is able to interact with the cell receptors;
- d) calculating changes in <u>complex</u> impedance for each frequency by subtracting the <u>complex</u> impedance for the reference time point from the <u>complex</u> impedance for each <u>time point</u> subsequent <u>to the reference</u> time point;
- e) parameterizing the changes in <u>complex</u> impedance for each time point, receptor, and stimulus;
- f) and, comparing the parameterized changes in impedance to parameter sets of known messenger pathways to assigning the parameterized changes in complex impedance to a known stimulus/receptor interaction class.

Claim 13 (Currently amended). The method of claim 12, further comprising the steps of

g) measuring the complex impedance over at least one frequency within a range of

frequencies for each time point during a selected period of time for the electrical circuit

comprising a-cells with a known receptor type;

h) selecting a reference time point corresponding to a time period immediately prior to

addition of an unknown stimulus;

i) adding the unknown stimulus to the electrical circuit such that the stimulus is able to

interact with the cell receptors;

j) calculating changes in the complex impedance for each frequency by subtracting the

value of the impedance for the reference time point from the value of the impedance for

each subsequent time point after subsequent to addition of the unknown stimulus;

k) parameterizing the changes in complex impedance for each time point, receptor, and

stimulus;

l) comparing the <u>parameterized</u> changes in the <u>complex</u> impedance after addition of the

unknown stimulus to the parameterized changes in the complex impedance for known

stimuli to correlate the parameterized changes in the complex impedance to a cellular

response;

m) and, assigning the cellular response to a known substance/receptor interaction class and

classifying the stimulus.

Claim 14 (Currently amended).

The method of claim 12, further comprising the steps of

a) measuring an the complex impedance over at least one frequency within a range of frequencies for each time point during a selected period of time for a the electric circuit comprising cells with an unknown receptor type;

- b) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus with a known response;
- c) adding the stimulus to the electrical circuit such that the stimulus is able to interact with the cell receptors;
- d) calculating changes in <u>complex</u> impedance for each frequency by subtracting the <u>complex</u> impedance for the reference time point from the complex impedance for each <u>subsequent</u> time point <u>subsequent to after</u> addition of the stimulus;
- e) parameterizing the changes in complex impedance for each time point, receptor, and stimulus;
- f) comparing the <u>parameterized</u> changes in <u>complex</u> impedance after addition of the stimulus to the <u>parameterized</u> changes in <u>complex</u> impedance for known receptors to correlate the parameterized changes in <u>complex</u> impedance to a cellular response;
- g) and, assigning the cellular response to a known substance/receptor interaction class and classifying the receptor.

Claim 15 (Canceled).

Claim 16 (Currently amended). The method of claim 12, wherein the changes in complex impedance are measured as resistance or reactance.

Page 9

Claim 17 (Currently amended). The method of claim 12, wherein the changes in complex impedance are measured as admittance, conductance, or susceptance.

Claim 18 (Currently amended). The method of claim 12, wherein the at least one frequency of the electromagnetic spectrum in a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

19 (Currently amended). The method of claim 12, wherein the range of frequencies is 40Hz to 110MHz.

Claim 20 (Currently amended). The method of claim, wherein the stimulus is a substance.

Claim 21 (Canceled).

Claim 22 (Currently amended). The method of claim 20, wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

Claim 23 (Canceled).

36 (Canceled).

37 (Canceled).